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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/517,702

08/02/2005

Koji Sode

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07/31/2006

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER

MEAH, MOHAMMAD Y

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 07/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/517,702

Applicant(s)

SODE, KOJI

Examiner

Mohammad Meah

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 2,3,6-13 and 18-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,5,14-17,29 and 30 is/are rejected.
- 7) ☐ Claim(s) 1,5,14-16,29 and 30 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3/8/05, 12/13/04, 5/12/06
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

With preliminary amendment of this application, the applicant, on date 05/08/2006 elected with traverse Group II (claims 1, 4-5, 14-17 and 29-30).

Election/Restriction

During preliminary amendment of this application, the applicant on date 05/08/2006 elected with traverse Group II (claims 1, 4-5, 14-17 and 29-30), drawn to modified glucose dehydrogenase comprising SEQ ID NO: 1, wherein Thr366 and Asp167 of SEQ ID NO: 1 are replaced, for examination. Groups I, III-XIII (claims 2-3, 6-13, 18-28) of election/restriction-office action of date 02/25/2006 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Applicants argument that Yoshida (cited during election/restriction-office action of date 02/25/2006) do not disclose exactly the same technical feature of their invention is persuasive however Applicants argument of the claims are linked by a special technical feature still is not persuasive because Kaneko et al. (Accession NO S74981) teach a gene encoding glucose dehydrogenase which has 15% sequence identity with SEQ ID NO: 1 and having one or more amino acid residues in the region of 349-377 (Cys369 by Trp369) of SEQ ID NO: 1 is replaced and Asp167 is also replaced by Gln (Gln167). Further evidence for not having special technical feature is shown in the 102/103-rejection below. Therefore restriction is maintained. And made FINAL.

Priority

Acknowledgement is made of applicant's PCT priority date based on application filing date of 06/13/2003 in Japan # PCT/JP03/07542 and foreign application JAPAN 2002-172955 06/13/2002, JAPAN 2003-71744 03/17/2003.

Claim Objections

Claim 5 is objected in recitation of "asparagines." It should be "asparagine."

Appropriate correction is required.

Claims 1, 14-16, 29-30 are objected for containing non-elected subject matters.

Appropriate correction is required.

Claim Rejections

35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out

And distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 4-5, 14-17 and 29-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-5, 14-17 and 29-30 are rejected because of the amino acid position Nos in the claims and specification do not match with the amino acid position Nos in the SEQ ID NO: 1 in the sequence listing which makes all claimed inventions indefinite and confusing. Position 366 in SEQ ID NO: 1 is actually Lys not Thr. **Is "Thr366 recited in claims" Thr342 in the SEQ ID NO: 1?** For purpose of further examination this is presumed.

Claims 1, 14, 29-30- "in a region of 349-377 amino acid of water soluble PQQGDH derived from *Acinebacter calcoaceticus*" is confusing as it is unclear if claim is limited to mutants of *Acinebacter calcoaceticus* PQQGDH and it is unclear as written that the number refer to amino acid positions that are mutated. It can be made clear by reciting "wherein one or more of amino acid residues 349-377 of--"

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 14 and 29-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to any modified pyrroloquinoline quinine glucose dehydrogenase (PQQGDH) derived from *Acinetobacter calcoaceticus* wherein any amino acid residue from region 349-377 of PQQGDH are modified. The specification teaches the structure of only a few representative species of such glucose dehydrogenase variants. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than having inhibition constant of 200 mM or more. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1, 14 and 29-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modified PQQGDH of SEQ ID NO: 1 wherein Thr366 (or Thr342) and Asp167 (Asp143) are replaced by other amino acids, does not reasonably provide enablement for any modified PQQGDH derived from *Acinetobacter calcoaceticus* PQQGDH wherein any amino acid is modified from amino acid residue from region 349-377 and have inhibition constant of 200 mM or

more. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1, 14 and 29-30 are so broad as to encompass any PQQGDH) derived from *Acinetobacter calcoaceticus* wherein any amino acid is modified from amino acid residue from region 349-377 and have inhibition constant of 200 mM or more. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of oxidoreductase or glucose dehydrogenase variants broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of only a few PQQGDH variants.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

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modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification while describe the mutation of two amino acid residues (i.e. Thr366 (or Thr342) and Asp167 (Asp143)) from 349-377 amino acid residues of SEQ ID NO: 1 does not support the broad scope of the claims which encompass any PQQGDH) derived from *Acinetobacter calcoaceticus* wherein any amino acid is modified from amino acid residue from region 349-377 and have inhibition constant of 200 mM or more because the specification does not establish: (A) structure of PQQH protein wherein region 349-377 of the SEQ ID NO: 1 be modified to attain desired inhibition constant; (B) the general tolerance of PQQGDH to modification of region 349-377 of the SEQ ID NO: 1 and extent of such tolerance; (C) a rational and predictable scheme for modifying any residue from region 349-377 of the SEQ ID NO: 1 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any PQQGDH) derived from *Acinetobacter calcoaceticus* wherein any amino acid is modified from amino acid residue from region 349-377 and have inhibition constant of 200 mM or more. The scope of the claims must bear a reasonable correlation with the scope of enablement

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(In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of oxidoreductase variants, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988).

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 29-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Breton et al. (US PAT 6562958).

Breton et al. teaches an amino acid sequence derived from *Acinetobacter calcoaceticus* having 95% sequence identity with applicant's SEQ ID NO: 1 and in said protein Thr342 ("Thr366") is replaced by A366. Although Breton et al. does not disclose the co-factor specificity of the disclosed enzyme, co-factor specificity is a property

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inherent in the structure of the protein. In view of the 95% sequence identity of Breton's enzyme to the PQQGDH sequence of the application (i.e. SEQ ID NO:1), and in view of the fact that said enzyme isolated from same source, a skilled artisan would expect that the protein of Breton et al would have the same co-factor specificity as the protein of SEQ ID NO: 1 of the present application.

Since the office does not have facilities to test the characteristics of a prior protein and reasonable basis exists for believing that the prior art protein has all the recited characteristics, it is the burden of the applicant to show that the prior art protein lacks the characteristics.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

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more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Mohammad Younus Meah, PhD

Examiner, Art Unit 1652

Recombinant Enzymes, 3C31 Remsen Bld

400 Dulany Street, Alexandria, VA 22314

Telephone: 517-272-1261


REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1600
1600